

**REMARKS**

Reconsideration and allowance of the subject application are respectfully requested.

Claims 8, 9 and 10-13 are pending in this application. Claims 4, 6 and 7 have been cancelled. Claims 10-13 have been added. The applicants note that claim 8 has been found to be allowable.

The applicants respectfully traverse the rejection of claims 6, 7 and 9 under 35 USC 103(a) in view of Asami et al. This reference does not make the presently claimed invention to be obvious.

Asami discloses that astaxanthin and/or its ester is an effective ingredient for an anti-stress composition, and that stress disorders and other related disorders are believed to result in an inability of the body to maintain homeostasis.

The Examiner acknowledges at page 3, section 4, that Asami does not teach employing an astaxanthin containing composition for treating a patient having a disturbance of circadian rhythm.

Please note that claim 9 has been amended to clarify that the recitation "suppressing degradation of in vivo melatonin" is an important feature of the claimed invention and in view of the Examiner's comments, the feature has been repeated within the body of the claim.

Asami discloses in the working examples of the specification that astaxanthin was orally administered to test mice, and that the mice were then restrained for 20 hours in metal restraint cages under conditions of minimal body movement and minimal access to drinking water to induce restraint stress.

The test mice were sacrificed and observed with respect to suppression effects on the reduction of immunological function and of cancer metastasis and accentuation.

In contrast, for the present invention, the circadian rhythm normalizing activity of astaxanthin or astaxanthin plus melatonin was determined and confirmed by experimentation with rats that were kept under stress-free conditions. Specifically, measurements were performed of daily movements of rats that were fed under normal conditions and kept free from stress, as shown in the examples of the specification for the present application. The tests were conducted to determine improvements in or normalizing of circadian rhythm with representative test animals which were fed under stress-free conditions. However, the experiment was not conducted to determine normalization of disturbance of circadian rhythm caused by stress.

Thus, the applicants submit that a person of ordinary skill in the art would understand that the mechanism for normalizing circadian rhythms according to the present invention significantly differs from that for preventing or alleviating decreased immunological function caused by stress as disclosed in Asami.

Accordingly, the applicants submit that the presently claimed invention is not obvious from the teachings of Asami.

Importantly, the applicants further point out the new and unexpectedly good results attained by the presently claimed invention with use of a combination of astaxathin and melatonin on the basis of the Example 2 of the specification and shown in Figure 5. The activity for normalizing circadian rhythms by administration

of astaxanthin and melatonin is evaluated in terms of the ratio of movements in light period. The results, shown in Figure 5, are as follows:

(a)	Control:	31.8%
(b)	Melatonin alone:	29.9%
(c)	Astaxanthin alone	27.6%
(d)	Astaxanthin + Melatonin	22.5%

From the test results, the value of (b) was decreased by 1.9% compared to (a), the control. The value of (c) was decreased by 4.2% compared to (a). It can be expected from the values of (b) and (c) that the value of (d) would be about 6% if the combination of astaxanthin and melatonin (d) performs the additive effect. However, the value of (d) compared to the control (a) was decreased by 9.3% which indicates a value about 1.5 times higher than that expected. It is therefore clear that the combination of astaxanthin with melatonin exhibited synergistic effects.

Accordingly, the applicants submit that the presently claimed invention is nowhere disclosed, suggested or made obvious by the teachings of Asami. The presently claimed invention is fully allowable in view of the cited references.

The applicants respectfully traverse the rejection of claim 4 under 35 USC 103(a) in view of Asami et al. taken with Pierpaoli et al. The cited reference does not make the presently claimed invention to be obvious.

However, please note that claim 4 has been cancelled, thus rendering this rejection to be moot.

In view of the above, it is believed that this application is in condition for allowance and a Notice to that effect is respectfully requested.

Respectfully submitted,

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